WASHINGTON WORKS
TEFLON® DIVISION

AR226-1623

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September 28, 1982

TO: R. J. ZIPFEL

FROM: J. G. LOSCHIAVO J.G.L.

AMMONIUM PERFLUOROOCTANOATE (C-8) IN BLOOD OF TEFLON® EMPLOYEES

References: (1) Letter, T. P. Pastoor to J. G. Loschiavo, 8/25/82, this subject, attached.
(2) Letter, J. G. Loschiavo to R. J. Zipfel, 7/29/82, this subject, attached.

The purpose of this letter is to summarize and comment on the two reference letters. I initially estimated that 40% of inhaled C-8 vapor is retained in the blood. The remaining 60% of inhaled vapor has four fates:

- It is immediately exhaled.
- It is inhaled but not absorbed into the body.
- It is eliminated by the kidneys, intestines, and sweat glands.
- It is retained in other body tissues besides blood.

I asked T. P. Pastoor, a Haskell Laboratory Toxicologist, to review my calculations. He used a somewhat different approach but came up with similar results. He estimated the fraction of inhaled C-8 vapor that is retained in the entire body. I, on the other hand, estimated the fraction of inhaled C-8 retained only in the blood.

AJP001237

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It has been estimated from data collected on female employees transferred out of TEFLON®, that it takes about 420 days for the body to eliminate half of accumulated C-8 (t 1/2 = 420 days). Using the formula listed on page two of Pastoor's letter, it is estimated that 47% of inhaled C-8 is retained in the entire body. Since I estimated C-8 retention in blood, which contains a fraction of total body water, it is not surprising that Pastoor's estimation is somewhat higher. Most importantly, both approaches indicate that much less than 100% of inhaled C-8 vapor is retained in the blood. Pastoor estimated that only about one-half of inhaled C-8 vapor is retained in the entire body. This is indeed encouraging. These estimations are rough since they are based on data from only four employees. Pastoor recommends that more human blood C-8 data be collected in order for more accurate estimations to be made. A greater effort is now being made to gather such data.

Attachments

JGL/nsw
1044W-2

ES-3575 REV. 8-81

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August 25, 1982

PERSONAL AND CONFIDENTIAL

J. G. LOSCHIAVO
POLYMER PRODUCTS DEPARTMENT
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AMMONIUM PERFLUOROOCTANOATE (C-8)
IN HUMAN BLOOD

In reference to your July 29, 1982, letter to R. J. Zipfel (Retention of Ammonium Perfluorooctanoate [C-8] in Blood of Teflon® Workers) I would like to make several important suggestions. Acquisition and interpretation of C-8 blood concentrations in workers is very important in understanding how the human body handles C-8 and how accurately our animal models at Haskell correlate to the human situation. To better interpret these data, consider the following modifications:

- The 0.006 ppm blood level is termed a "rate" of accumulation when it would be more appropriate to call it an "average concentration" over the average of 91 days of employment. The average blood level of 0.006 ppm/day x 91 days gives the plateau, or steady-state, concentration (0.546 ppm) that more closely represents the dynamic aspects of exposure and elimination.

- The calculations assume a volume of distribution (Vd) equal to the blood compartment only (5.5 liters). Since C-8 is water soluble and binds protein, the Vd would actually be closer to the volume of total body water (approximately 42 liters/70 kg man).

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- To more accurately assess the retention of C-8 in the body as well as predict blood levels anticipated with continued low-level exposure, formulas commonly used to estimate drug-therapy regimen can be employed.

  Assumptions:

  - The blood level, Cp, is at a plateau (steady-state) concentration (i.e., absorption and elimination approximately equal).
  - The volume of distribution, Vd, is in total body water, or 42 liters.
  - The daily dose (D/T) is 0.081 mg/day.
  - The elimination half-life, t 1/2, is estimated from a literature report on one individual. The value is 655 days, but could vary considerably.

  Then from Goodman and Gilman (1970):

$$Cp = \frac{f \bullet 1.44 \bullet t\ 1/2}{Vd} \left(\frac{D}{T}\right)$$

  - where f = fraction absorbed
  - solving for f,

$$f = \frac{Cp \bullet Vd \bullet T}{1.44 \bullet t\ 1/2 \bullet D} = \frac{0.546\ mg/l \bullet 42\ell \bullet 1\ day}{1.44 \bullet t\ 1/2 \bullet 0.081\ mg/\ell}$$

  - then:

| t 1/2 (days) | f | % Absorbed |
|---|---|---|
| 30 | 6.55 | 655 |
| 197 | 1.00 | 100 |
| 360 | 0.55 | 55 |
| 655 | 0.30 | 30 |

- Thus, depending on the actual t 1/2, we can estimate only that greater than 30% of atmospheric C-8 is absorbed. This is in general agreement with your estimate, but until we know the actual t 1/2 we will not be able to accurately calculate fractional absorption.

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- Regarding these calculations and in response to your suggestions in the July 29 memorandum,

  - More human data is necessary from two sources:

    1. current employees for determination of plateau (steady-state) concentrations
    2. employees no longer exposed to C-8 for determination of the blood t 1/2, and the urinary excretion rate.

  - We have performed radiochemical and biochemical analysis of the distribution and effects of C-8.

Timothy P. Pastoor

TIMOTHY PJ PASTOOR
RESEARCH TOXICOLOGIST

TPP:sgl

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PERSONAL AND CONFIDENTIAL

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July 29, 1982

TO: R. J. ZIPFEL

FROM: J. G. LOSCHIAVO J.G.L.

RETENTION OF AMMONIUM PERFLUOROOCTANOATE (C-8)
IN BLOOD OF TEFLON® EMPLOYEES

Using data from the FLAIR* program and from air sampling records, it is estimated that 40% of inhaled C-8 vapor is retained in the blood (see attachment). This estimate is rough since it is based on only four data points. Also, the rate of C-8 absorption varies by individual. Air C-8 levels are also variable.

Data on males only were used due to potential sex differences in C-8 absorption and elimination as observed in rat studies. Data on Fine Powder/Dispersion employees only were used to eliminate the variable of particle size. In areas where a significant portion of airborne C-8 is contained in polymer particles, blood retention should be less than 40% of inhaled C-8. This reduced blood C-8 retention is due to the airborne particle size distribution. Large particles (i.e., particles > 5 microns in diameter) will not likely reach the lung alveolar region. It is in the alveolar region where inhaled gases and vapors are absorbed into the blood. Probably for this reason, TEFLON® FEP Operators have significantly lower blood C-8 levels than Fine Powder/Dispersion Operators.

According to G. L. Kennedy, Haskell Laboratory Toxicologist, not more than 20% of inhaled C-8 accumulates in body tissues besides blood. Rat studies indicate that 10 to 20% of inhaled C-8 is pooled or accumulated by other body tissues.

*FLAIR - Fluoropolymers Laboratory Analysis Information Retrieval.

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AJP001242

EID080642

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The remaining 40% of inhaled C-8 has 3 potential fates:

- o It is exhaled back out.
- o It is inhaled but not absorbed into the body.
- o It is eliminated by the kidneys or intestines.

The following additional information is needed to determine more accurately the fate of inhaled C-8:

- o More blood C-8 data on males who left TEFLON®.
- o More blood C-8 data on new male TEFLON® employees.
- o More blood C-8 data on new female TEFLON® employees.
- o Data on amount of C-8 excreted over a 24-hour period following exposure.
- o Particle-size distribution of airborne polymer particles containing C-8.
- o Perform a Haskell Laboratory study using radiolabelled C-8 to determine where and how much C-8 is stored in the body immediately after exposure.
- o Data on C-8 content in exhaled air during exposure.

Attachment

JGL/nsw
0885W-2

AJP001243

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## CALCULATIONS AND DATA

Blood C-8 accumulation rates in four male Fine Powder/Dispersion Operators with less than 550 days of service are as follows:

0.0093 ppm C-8 in blood/workday
0.0080 ppm C-8 in blood/workday
0.0043 ppm C-8 in blood/workday
0.0022 ppm C-8 in blood/workday

$\overline{X} = 0.0060$

Personal air sample results in moles per billion (mpb) C-8 on these Operators during the same period are:

<0.03, 0.09, 0.12, 0.12, 0.15, 0.24, 0.24, 0.66, 0.69, 0.73, 0.75, and 1.39

$\overline{X} = 0.46$ mpb or 8.2 ug./m3

Average male has 5,500 gm. of blood in his body and inhales 10 $m^3$ of air over an 8-hour shift doing light work.(1)

At a C-8 concentration of 0.46 mpb (8.1 ug./$m^3$), an average male would inhale 81 ug. of C-8 during an 8-hour shift.

If all C-8 inhaled was retained in the blood, an average male would accumulate C-8 in blood at a rate of:

$$\frac{81 \text{ ug. C-8/workday}}{5.5 \times 10^9 \text{ ug. blood}} \times 10^6 = 0.0147 \frac{\text{ppm C-8 in blood}}{\text{workday}}$$

However, the average daily C-8 accumulation rate we observe in new employees is only 0.0060 $\frac{\text{ppm C-8 in blood}}{\text{workday}}$. Therefore, of the total C-8 inhaled, about $\left(\frac{0.0060}{0.0147} \times 100 = 40\%\right)$ 40% is retained in blood.

(1) Radiological Health Handbook, U.S. Department of Health, Education, and Welfare; Revised Edition, January, 1970, (pp. 215 and 216).

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